Amendments To The Claims

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of the claims

- Claim 1. (Currently amended) A method of *ex-vivo* expanding stem and/or progenitor cells, while at the same time, substantially inhibiting differentiation of the stem and/or progenitor cells, the method comprising:
- (a) obtaining a population of cells comprising stem and/or progenitor cells;
- (b) seeding said stem and/or progenitor cells into a <u>stirred flask or rotating</u> wall vessel bioreactor, and
- (c) culturing said stem and/or progenitor cells *ex-vivo* in said bioreactor without stromal cells or a feeder layer, under conditions allowing for cell proliferation and, at the same time, culturing said cells in the presence of a copper chelator under conditions selected from the group consisting of:
- (i) conditions reducing expression and/or activity of CD38 in said cells;
- (ii) conditions reducing capacity of said cells in responding to signaling pathways involving CD38 in said cells;
- (iii) conditions reducing capacity of said cells in responding to retinoic acid, retinoids and/or Vitamin D in said cells;
- (iv) conditions reducing capacity of said cells in responding to signaling pathways involving the retinoic acid receptor, the retinoid X receptor and/or the Vitamin D receptor in said cells;
- (v) conditions reducing capacity of said cells in responding to signaling pathways involving PI 3-kinase;
- (vi)—conditions wherein said cells are cultured in the presence of nicotinamide, a nicotinamide analog, a nicotinamide or a nicotinamide analog derivative or a nicotinamide or a nicotinamide analog metabolite;

- (vii) conditions wherein said cells are cultured in the presence of a copper chelator;
- (viii) conditions wherein said cells are cultured in the presence of a copper chelate;
- (ix) -- conditions wherein said cells are cultured in the presence of a PI 3-kinase inhibitor;

thereby expanding <u>said</u> the stem and/or progenitor cells while at the same time, substantially inhibiting differentiation of <u>said</u> the stem and/or progenitor cells *ex-vivo*, wherein said copper chelator is tetraethylenepentamine and wherein said providing said conditions for cell proliferation is effected by providing the cells with early-acting cytokines.

- Claim 2. (Currently amended) The method of claim 1, wherein said stem and/or progenitor cells are derived from a source selected from the group consisting of hematopoietic cells, umbilical cord blood cells, G-CSF mobilized peripheral blood cells and [[,]] bone marrow cells, hepatic cells, pancreatic cells, intestinal cells, neural cells, oligodendrocyte cells, keratinocytes, skin cells, muscle cells, bone cells, chondrocytes and stroma cells.
- Claim 3. (Original) The method of claim 1, further comprising the step of selecting a population of stem cells enriched for hematopoietic stem cells.
- Claim 4. (Original) The method of claim 3, wherein said selection is affected via CD34.
- Claim 5. (Original) The method of claim 1, further comprising the step of selecting a population of stem cells enriched for early hematopoietic stem/progenitor cells.
- Claim 6. (Original) The method of claim 5, wherein said selection is affected via CD133.
- Claim 7. (Original) The method of claim 1, wherein step (b) is followed by a step comprising selection of stem and/or progenitor cells.

Claim 8. (Original) The method of claim 7, wherein said selection is affected via CD 133 or CD 34.

Claim 9-10. (Canceled)

- Claim 11. (Currently amended) The method of claim [[10]]1, wherein said early acting cytokines are selected from the group consisting of stem cell factor, FLT3 ligand, interleukin-6, thrombopoietin and interleukin-3.
- Claim 12. (Withdrawn) The method of claim 10, wherein said late acting cytokines are selected from the group consisting of granulocyte colony stimulating factor, granulocyte/macrophage colony stimulating factor and erythropoietin.
- Claim 13. (Withdrawn) The method of claim 10, wherein said late acting cytokine is granulocyte colony stimulating factor.
- Claim 14. (Original) The method of claim 1, wherein said stem and/or progenitor cells are genetically modified cells.
- Claim 15. (Withdrawn) The method of claim 1, wherein said inhibitors of PI 3-kinase are wortmannin and/or LY294002.

Claim 16. (Canceled)

- Claim 17. (Withdrawn) The method of claim 16, wherein said static bioreactor is selected from the group consisting of well plates, tissue-culture flasks and gas-permeable culture bags.
- Claim 18. (Original) The method of claim 1, wherein said culturing said cells of step (c) is effected in suspension culture.
- Claim 19. (Original) The method of claim 1, wherein said culturing said cells of step (c) is effected on a porous scaffold.

- Claim 20. (Original) The method of claim 19, wherein said porous scaffold is selected from the group consisting of poly (glycolic acid), poly (DL-lactic-co-glycolic acid), alginate, fibronectin, laminin, collagen, hyaluronic acid, Polyhydroxyalkanoate, poly 4 hydroxybutirate (P4HB) and polygluconic acid (PGA).
- Claim 21. (Original) The method of claim 19, wherein said porous scaffold comprises a hydrogel.
- Claim 22. (Original) The method of claim 1, wherein said seeding is static seeding or perfusion seeding.

Claim 23. (Canceled)

- Claim 24. (Withdrawn) A conditioned medium isolated from the expanded stem and/or progenitor cell culture of claim 1.
- Claim 25. (Withdrawn) A method of preparing a stem and/or progenitor cell conditioned medium, the method comprising:
- (a) establishing a stem and/or progenitor cells culture in a bioreactor according to claim 1, thereby expanding the stem and/or progenitor cells while at the same time, substantially inhibiting differentiation of the stem and/or progenitor cells *ex-vivo*; and
- (b) when a desired stem and/or progenitor cell density has been achieved, collecting medium from said bioreactor, thereby obtaining the stem and/or progenitor cell conditioned medium.
- Claim 26. (Withdrawn) The stem and/or progenitor cell conditioned medium of claim 25.
- Claim 27. (Withdrawn) A method of transplanting *ex-vivo* expanded stem and/or progenitor cells into a recipient, the method comprising:

- (a) obtaining a population of cells comprising stem and/or progenitor cells;
 - (b) seeding said stem and/or progenitor cells into a bioreactor, and
- (c) culturing said stem and/or progenitor cells *ex-vivo* in said bioreactor under conditions allowing for cell proliferation and, at the same time, culturing said cells under conditions selected from the group consisting of:
- (i) conditions reducing expression and/or activity of CD38 in said cells;
- (ii) conditions reducing capacity of said cells in responding to signaling pathways involving CD38 in said cells;
- (iii) conditions reducing capacity of said cells in responding to retinoic acid, retinoids and/or Vitamin D in said cells;
- (iv) conditions reducing capacity of said cells in responding to signaling pathways involving the retinoic acid receptor, the retinoid X receptor and/or the Vitamin D receptor in said cells;
- (v) conditions reducing capacity of said cells in responding to signaling pathways involving PI 3-kinase;
- (vi) conditions wherein said cells are cultured in the presence of nicotinamide, a nicotinamide analog, a nicotinamide or a nicotinamide analog derivative or a nicotinamide or a nicotinamide analog metabolite;
- (vii) conditions wherein said cells are cultured in the presence of a copper chelator;
- (viii) conditions wherein said cells are cultured in the presence of a copper chelate;
- (ix) conditions wherein said cells are cultured in the presence of a PI 3-kinase inhibitor; and
- (d) recovering said expanded stem and/or progenitor cells from said bioreactor, and
- (e) transplanting into said recipient said ex-vivo expanded stem and/or progenitor cells produced in steps (b)- (d).

- Claim 28. (Withdrawn) The method of claim 27, wherein said stem and/or progenitor cells are derived from a source selected from the group consisting of hematopoietic cells, umbilical cord blood cells, G-CSF mobilized peripheral blood cells, bone marrow cells, hepatic cells, pancreatic cells, intestinal cells, neural cells, oligodendrocyte cells, skin cells, keratinocytes, muscle cells, bone cells, chondrocytes and stroma cells.
- Claim 29. (Withdrawn) The method of claim 27, further comprising the step of selecting a population of stem cells enriched for hematopoietic stem cells.
- Claim 30. (Withdrawn) The method of claim 29, wherein said selection is affected via CD34.
- Claim 31. (Withdrawn) The method of claim 27, further comprising the step of selecting a population of stem cells enriched for early hematopoietic stem/progenitor cells.
- Claim 32. (Withdrawn) The method of claim 31, wherein said selection is affected via CD133.
- Claim 33. (Withdrawn) The method of claim 27, wherein step (c) is followed by a step comprising selection of stem and/or progenitor cells.
- Claim 34. (Withdrawn) The method of claim 33, wherein said selection is affected via CD 133 or CD 34.
- Claim 35. (Withdrawn) The method of claim 27, wherein said stem and/or progenitor cells of step (b) are obtained from said recipient.
- Claim 36. (Withdrawn) The method of claim 27, wherein said providing said conditions for cell proliferation is effected by providing the cells with nutrients and cytokines.
- Claim 37. (Withdrawn) The method of claim 36, wherein said cytokines are selected from the group consisting of early acting cytokines and late acting cytokines.

- Claim 38. (Withdrawn) The method of claim 37, wherein said early acting cytokines are selected from the group consisting of stem cell factor, FLT3 ligand, interleukin-6, thrombopoietin and interleukin-3.
- Claim 39. (Withdrawn) The method of claim 37, wherein said late acting cytokines are selected from the group consisting of granulocyte colony stimulating factor, granulocyte/macrophage colony stimulating factor and erythropoietin.
- Claim 40. (Withdrawn) The method of claim 39, wherein said late acting cytokine is granulocyte colony stimulating factor.
- Claim 41. (Withdrawn) The method of claim 27, wherein said stem and/or progenitor cells are genetically modified cells.
- Claim 42. (Withdrawn) The method of claim 27, wherein said inhibitors of PI 3-kinase are wortmannin and/or LY294002.
- Claim 43. (Withdrawn) The method of claim 27, wherein said bioreactor is selected from the group consisting of a static bioreactor, a stirred flask bioreactor, a rotating wall vessel bioreactor, a hollow fiber bioreactor and a direct perfusion bioreactor.
- Claim 44. (Withdrawn) The method of claim 43, wherein said static bioreactor is selected from the group consisting of well plates, tissue-culture flasks and gas-permeable culture bags.
- Claim 45. (Withdrawn) The method of claim 27, wherein said culturing said cells of step (c) is effected in suspension culture.
- Claim 46. (Withdrawn) The method of claim 27, wherein said culturing said cells of step (c) is effected on a porous scaffold.

- Claim 47. (Withdrawn) The method of claim 46, wherein said porous scaffold is selected from the group consisting of poly (glycolic acid), poly (DL-lactic-co-glycolic acid), alginate, fibronectin, laminin, collagen, hyaluronic acid, Polyhydroxyalkanoate, poly 4 hydroxybutirate (P4HB) and polygluconic acid (PGA).
- Claim 48. (Withdrawn) The method of claim 41, wherein said porous scaffold comprises a hydrogel.
- Claim 49. (Withdrawn) The method of claim 27, wherein said seeding is static seeding or perfusion seeding.
- Claim 50. (Withdrawn) The method of claim 27, wherein said culturing of said cells of steps (b) and (c) is effected without stromal cells or a feeder layer.